Environmental Science in the City That Never Sleeps

Editor's note: This article on the Environmental Health Sciences Center of the Mount Sinai School of Medicine is the seventh in a series that appears intermittently in NIEHS News.

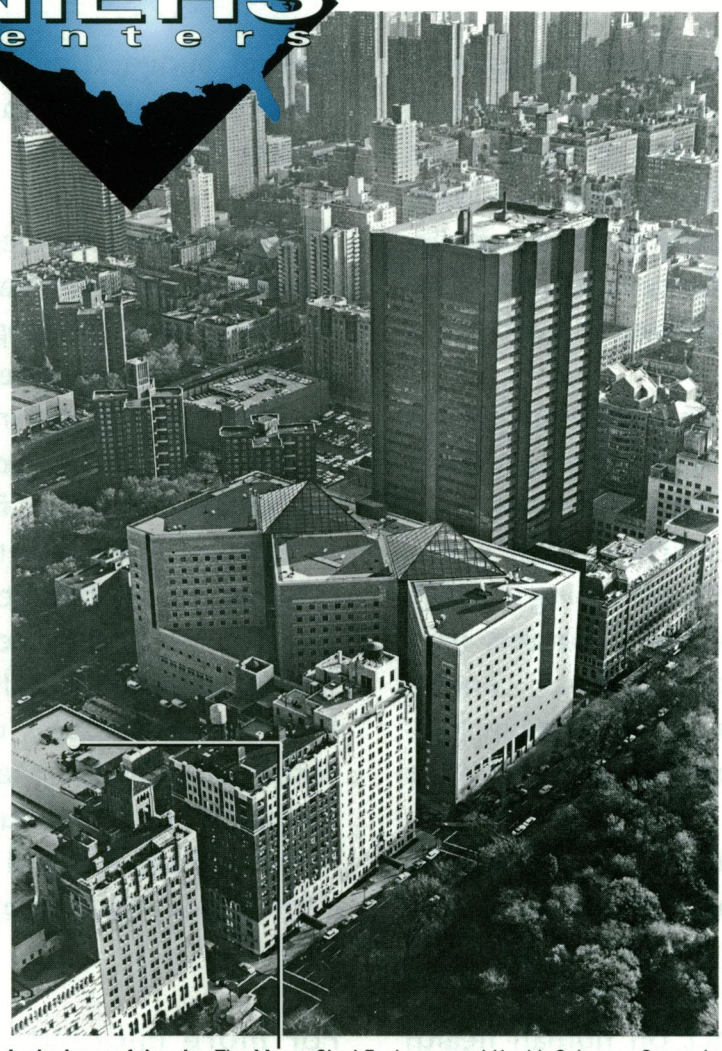
During the New York City building boom of the 1960s, midtown shoppers and office workers often joked about the "snow" that sometimes fell from a clear blue sky. The surreal-looking blizzards were, in fact, fluffy clusters of asbestos fibers, escaping from construction sites where the insulating material was being sprayed on steel beams in the skyscrapers under construction.

At the same time, at Mount Sinai Hospital on upper Fifth Avenue, a pulmonologist named Irving J. Selikoff knew that asbestos was nothing to laugh about and was determined to keep it out of the lungs of Americans.

In those days, hardly anyone, least of all the workers who handled asbestos or were exposed to it indirectly, saw any threat from the nearly invisible needle-shaped fibers, some less than 1 micron in diameter. Physicians considered the material inert, harmless to humans, and, because of its fireproof properties, a lifesaving boon to mankind.

But in his New Jersey clinical practice Selikoff had discovered in 1954 that an astonishingly high percentage of men who worked with asbestos developed mesothelioma, an otherwise rare cancer of the soft tissues around the lungs. And it appeared that even among smokers, a disproportionately high percentage of lung cancer patients had been occupationally exposed to asbestos.

In 1962, Selikoff began a long collaboration with E. Cuyler Hammond, the American Cancer Society's director of statistics and epidemiology. With the cooperation of the International Association of Heat, Frost Insulators, and Asbestos Workers, as well as manufacturers of asbestos-containing products, the Mount Sinai team conducted some of the earliest and most influential studies of environmental carcinogenesis. The first of these studies was published in 1964 in the *Journal of the American Medical Association*. From the laboratory, the clinic, and the computer center, the Mount Sinai team went to the workplaces and even the homes of workers, where they found an elevated risk of lung cancer even for the wives who washed their husbands' asbestos-dusted work clothes.



Mount Sinai EHSC

In the heart of the city. The Mount Sinai Environmental Health Sciences Center is located near Central Park in the heart of the community it serves.

In 1961, the Mount Sinai Hospital named Selikoff the first director of its new Environmental Sciences Laboratory, which would later become the basis for the Mount Sinai Environmental Health Sciences Center. From this position, Selikoff argued consistently for threshold standards for asbestos to be established and enforced. It took years for government, business, and the public to take his warnings seriously; not until 1971 did the Occupational Safety and Health Administration (OSHA) put forth the first standards of consequence; even then, the limit of five fibers per milliliter of air was far below the recommendation of the American Conference of Governmental Industrial Hygienists. Today, the limit is one-fiftieth of the level set in 1971.

Established Traditions

Mount Sinai began as a rather fashionable urban hospital on the upper east side of Manhattan. Its prime site overlooking Central Park was flanked by elegant apartment buildings and museums, but only a few blocks away the New York Central railroad tracks emerged from underground, and the tone of the area changed dramatically to a middle-class neighborhood of apartment houses and retail stores. After World War II, many residents of the area near Mount Sinai moved to the suburbs, to be replaced by working people from the rural South and Puerto Rico. By 1967, when the hospital's medical school was founded as part of the City University of New York, deteriorating housing stretched from just a block to the east of Fifth Avenue for more than a mile to the East River. Urban problems were taking hold, and increasing numbers of residents crowded into the emergency room.

The changing social and physical environment of its neighborhood prompted Mount Sinai to form the first urban department of community medicine in the United States, which became the home of the Environmental Sciences Laboratory. Selikoff and his colleagues had demonstrated the importance of a multidisciplinary approach to environmental health research. The laboratory now enjoyed the resources of both a major clinical facility and a bustling medical school.

In 1973, The Mount Sinai Environmental Health Sciences Center was formed and received its first center core funding from the NIEHS. As one of the nation's

oldest environmental health research units, the center retains its original emphasis on human health and epidemiology in the urban environment and its dedication to investigating associations between environmental factors, particularly toxicants, and human disease. During its first 12 years as an NIEHS core center, Mount Sinai became renowned for delineating the hazards of lead, solvents, vinyl chloride, polychlorinated biphenyls (PCBs), and polybrominated biphenyls (PBBs).

New Directions

In 1985, Selikoff stepped down from his administrative duties, and the center's directorship passed to Philip J. Landrigan, a pediatrician with extensive public health experience in Africa and Central America, and many years of service in the U. S. Public Health Service, both at the Centers for Disease Control and at the National Institute for Occupational Safety and Health (NIOSH).

While maintaining the momentum of the Selikoff years, Landrigan has devoted the past decade to building the center's strength in analytical environmental epidemiology and in areas of basic science relevant to environmental health. The center has brought in new faculty members in epidemiology, biostatistics, biochemistry, neurobiology, medical genetics, physics, and molecular biology.

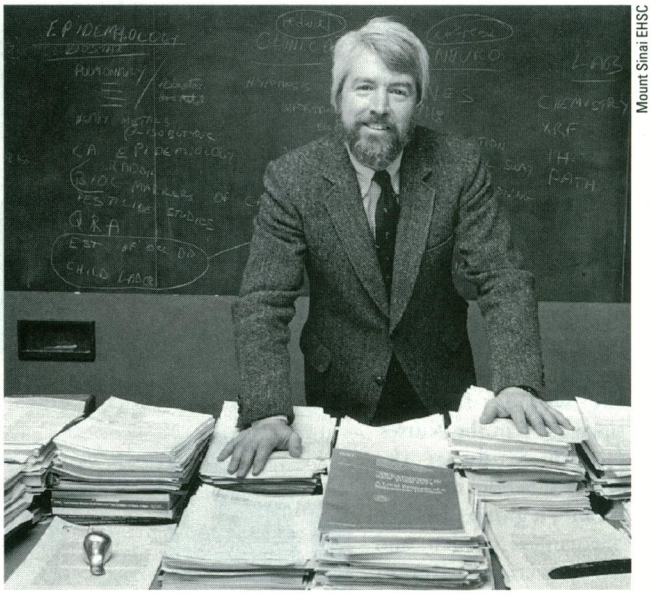
In addition, Landrigan forged stronger ties with the Mount Sinai School of Medicine, drawing in senior scientists from departments of clinical medicine and basic science to become active members of the center and collaborators in its research. Landrigan continues as an active investigator in his own field, lead toxicology.

In the past three years, the Mount Sinai center has been reorganized and now comprises three research cores devoted to heavy metals, environmental carcinogenesis, and women's environmental health research; three service and support cores of biometry, exposure assessment, and clinical/occupational medicine; a community outreach and education core coordinated by an administration core; and a pilot project program.

Heavy Metals

The multidisciplinary heavy metals core brings together epidemiologists, occupational physicians, physicists, geneticists, and neurotoxicologists from several departments within Mount Sinai. At present, the heavy metals core concentrates exclusively on lead. Its key resource is the X-ray fluorescence (XRF) system, which measures with great precision the amount of lead retained in bone. Andrew C. Todd, a medical physicist who helped develop XRF technology, conducts noninvasive tests with the device.

Landrigan and Todd are the principal investigators of an NIEHS-funded prospective study of the neuroepidemiology of lead, which is following young adults recently hired to work in bridge maintenance and other elements of New York City's infrastructure. De-spite respirators and other protective gear, these workers will be exposed to lead in paint used on structures built years ago. Researchers hope the long-term study will tell them whether the low levels of lead are harmful.



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Philip J. Landrigan. Protecting the community's health is the director's first priority.

James G. Wetmur, professor of microbiology and human genetics, is conducting a research project on the role of genetic polymorphism in response to environmental stressors. His work focuses on delta-aminolevulinic acid dehydratase (ALAD), an enzyme which decreases in activity during the early phases of lead poisoning. Some individuals have a variant form of the enzyme, which may increase the risk of adverse health effects if they are exposed to lead. Wetmur's group was the first to find a correlation between the presence of the gene that produces the abnormal enzyme and higher levels of lead in blood and the first to devise a polymerase chain reaction (PCR) method of recovering genetic information from small samples of blood.

Landrigan and Todd are also working on prospective epidemiologic studies to determine whether subclinical decreases in neurological function in women can be linked to occupational exposure to lead and whether low-level lead poisoning contributes to attention deficit/hyperactivity disorder in children.

Environmental Carcinogenesis

Mount Sinai's history of identifying and quantifying cancer-causing factors in the environment and the workplace continues in the environmental carcinogenesis core, directed by William J. Nicholson, a collaborator with Selikoff in many of the original studies of asbestos-related cancers.

With the advent of molecular biology and advanced statistical techniques, this core emphasizes integrating biological markers of exposure, carcinogenic effect, and susceptibility. The agents of interest are environmentally persistent organochlorines, radon, and asbestos.

One area of research in the environmental carcinogenesis core is distinguishing between the carcinogenic effects of the different types of asbestos fibers. Mount Sinai researchers have shown that chrysotile asbestos, touted by producers as safer than other forms, is a potent mesothelial carcinogen, although it is removed from the lung faster than other asbestos fibers. The concentration of chrysotile fibers is 50 or more times greater in mesothelium than in lung tissue, compared with amphibole asbestos fibers. Center scientists are studying genetic changes in mesothelioma with the goal of finding biomarkers that may lead to earlier detection of the malignancy.

Mary Wolff, director of the exposure assessment core, is conducting extensive research on the impact of environmental agents on breast cancer. Wolff has recently joined in a collaborative, congressionally mandated investigation to examine potential environmental factors that may account for the "epidemic" of breast cancer in nearby Long Island, where the incidence of the disease is the among the highest in the nation. Organochlorine pesticides were used in large amounts in Long Island during the 1950s and 1960s. Wolff will direct the analyses of organochlorines in the blood of 400 breast cancer cases and 400 controls. These levels will be correlated with geographic models estimating the participants' past environmental exposures to DDT, PCBs, chlordane, and polyaromatic hydrocarbons.

In a case–control study of breast cancer patients, Wolff studied the serum concentrations of PCBs and DDE, a by-product of DDT, taking diet, reproductive history, and prior breast disease into account, and

found that mean levels of both DDE and PCBs were higher among breast cancer cases than among their matched controls. In a related hospital-based case–control study, Wolff is seeking possible mechanisms linking organochlorines to breast cancer, and, with a number of collaborators, is looking at the same links in other populations—the women followed since 1976 in the Nurses' Health Study at the Harvard School of Public Health, a group of North Vietnamese women, and women from different ethnic groups in California enrolled in the Kaiser Permanente Medical Care Program. Using the same tools of molecular epidemiology, Wolff also hopes to undertake a study to determine whether these same compounds play a part in the etiology of prostate cancer.

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Words into action. Andrew Todd monitors the spectrum as an assistant positions the XRF machine to measure tibial bone lead in a subject.

In collaboration with scientists at the American Health Foundation, Ainsley Weston, deputy director of the Mount Sinai center, is examining the effects of PCBs and sediments from New York City waterways on normal human mammary epithelial cells. The project, supported by the Superfund, seeks to delineate the metabolism, activation, and DNA-adduct formation of benzo[*a*]pyrene and benzene, as well as endogenous estradiol, and to discover how this metabolism may be altered by individual and racial variations in normal human mammary epithelial cells. In a pilot study, Weston is working with Wolff to evaluate whether polymorphisms of cytochrome P450 and glutathione-*S*-transferase (both major carcinogen-metabolizing enzymes) are related to susceptibility to breast cancer in ethnic minorities.

Women's Environmental Health

The women's environmental health core was established in September 1994 as an extension of a working group that had been formed by Landrigan a year earlier. The working group had studied early pregnancy loss among women office workers by measuring urinary levels of follicle-stimulating hormone (FSH) as a marker of both ovarian toxicity and early pregnancy and had also studied the roles of DDE and PCBs in premature birth.

Epidemiologist Maureen Hatch was recruited from Columbia University to serve as the core's director. Hatch immediately brought in three new faculty members to extend the division's strength in reproductive epidemiology.

The unifying theme of this new research program is to study the effect of environmental toxicants on the health of women. Specifically, the core aims to assess the contributions of environmental factors to diseases of special importance to women, including breast and ovarian cancers, and gynecologic and obstetric problems; to trace the effects of female hormones on vulnerability to environmental toxicants, and to determine the effects of *in utero* exposure to environmental toxicants and maternal hormones on offspring.

The new core's first funded research projects began in April 1995, with support from Superfund. The center's XRF technology will be used to assess the release of lead from bone during pregnancy and lactation and during menopause. A study is also being planned to examine over 1500 blocks of tumor tissue from women diagnosed with breast cancer to look for mutations and overexpression of genes implicated in the disease.

Clinical/Occupational Medicine

The clinical/occupational medicine core provides expertise in assessing populations exposed to environmental toxicants and plays an important role in recruiting subjects. Stephen Levin, medical director of the Irving J. Selikoff Clinical Center, in Occupational and Environmental Medicine at Mount Sinai, is director of this core.

In 1974, the center began a clinic to complement its research program, which for years was New York City's only academically based occupational health clinical center. It developed many educational programs to help workers recognize and reduce their exposures to hazardous substances, such as asbestos education programs for members of the building trades and training for pest control workers in the health effects of pesticides. Research in the Clinical Center led to the recognition of lead exposure from firearms at shooting ranges used for police training and for recreation.

In 1987, at the request of the New York State Legislature, Landrigan and Steven Markowitz, assistant director of the Environmental Health Sciences Center, conducted a study of occupational disease in New York. They reported that occupational illness was the fourth most common cause of death in the state and estimated that the five most common occupational diseases cost over $600 million annually. Recognizing occupational disease as a major public health concern, the legislature created a network of occupational health clinical centers, coordinated by the New York State Department of Health and now funded by a surcharge on workers' compensation premiums.

Today, the Clinical Center sees over 3,000 patients yearly. It is equipped with spirometers and audiometers for screening. More elaborate pulmonary, neurological, and other tests are available through departments at Mount Sinai Hospital. The clinical center has access to a 15-bed inpatient unit within the hospital where clinical investigations can be carried out in depth on individuals exposed occupationally to lead and other agents, at no cost to the patients.

The center performs clinical investigations through the clinical core. An example is an ongoing study by Nicholson to determine whether the risk of cancer in insulation workers, heavily exposed to asbestos for 30 years or more, could be reduced by dietary factors, particularly beta-carotene. Nicholson has related various cancer risks to serum levels of vitamin A and beta-carotene, controlling for asbestos exposure and cigarette smoking, and has found decreasing trends in relative risk for all cancers, particularly lung cancer and gas-

trointestinal cancer, with increasing beta-carotene levels.

Community Outreach and Education

The community outreach and education core, directed by environmental neuroscientist Luz Claudio, was established in January 1995. Its goal is to educate community residents, workers, health care professionals, and policymakers about environmental health and disease prevention.

By serving as an information resource, the community outreach and education core hopes to foster environmental justice through communication with labor unions and community organizations, to encourage the teaching of occupational and environmental medicine in the medical school and in post-graduate medical curricula, and to draw more members of racial minorities into environmental health science careers.

Although this core is new, most of its activities are well-established at Mount Sinai. Under the Secondary Education Through Health program (SETH), the school of medicine has exposed over 3,000 high school students to opportunities in health careers, provided information on the influence of the environment and the workplace on health, and encouraged students to become knowledgeable health consumers. The SETH program recruits more than 200 students a year through cooperating junior and senior high schools for hands-on research, library research, seminars, instruction, and exposure to working in clinical and research environments. Ninety-five percent of SETH students are accepted by colleges. Three of Mount Sinai's SETH students were winners of the 1994 Westing-house Talent Search. Angela Diaz, a former SETH student, is director of Mount Sinai's Adolescent Health Center and is serng this year as a White House Fellow.

This program's success has led Mount Sinai to develop an environmental education component under a recent NIEHS Superfund basic science research grant. The project will offer a structured summer program for 15 minority students in the 11th and 12th grades and their teachers. The students will work with environmental scientists on projects involving heavy metals and chlorinated hydrocarbons. Students will also attend seminars on the history and philosophy of science and environmental medicine, study the Hudson River's ecology, and prepare presentations for weekly seminars. Researchers from all the cores at the center will serve as mentors to the students and the teachers will be trained in pedagogical methods shown to be effective in arousing students' interest in applying the scientific method to problems in the world around them.

In addition, researchers at the center are recruiting medical students to carry on the tradition of research in environmental health sciences. The center offers a summer research training program during which students work directly with faculty members on a specific research project. Students' time is spent attending seminars, observing patient sessions at the Occupational Health Clinical Center, and visiting work sites where they are introduced to a range of occupational and environmental health concerns. In the first four years of funding 22 students participated in the summer program. In keeping with one of the program's goals, 10 were members of racial and ethnic minority groups.

Although scientists at the Mount Sinai Environmental Health Sciences Center have an array of new technologies to address environmental health problems, they also have a strong sense of the mission of the center, supplied by Selikoff, Landrigan, and the other founding researchers, which is not only to conduct research and train new scientists and physicians, but also to ensure the long-term interests of the community in being free from environmental health hazards.

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Training tomorrow's scientists. Deputy Center Director Ainsley Weston works with technician Cindy Mao in the Environmental Molecular Biology Laboratory.

Naming Carcinogens

Scientists, consumer groups, manufacturers, and labor organizations recently debated the criteria for naming a chemical a carcinogen. The debate concerns *The Biennial Report on Carcinogens* (*BRC*), which lists known carcinogens and substances "reasonably anticipated" to be human carcinogens to which significant numbers of U.S. residents are exposed. In 1978, Congress mandated that the Department of Health and Human Services prepare these reports annually. In 1993, Congress changed the law to make the reports biennial. The seventh report was published in 1994. Now officials at the National Toxicology Program, which prepares the report, are determining if the criteria used to list chemicals need to be revised. One of the key questions is whether the NTP should consider mechanistic data—information on how chemicals work in the body and how cancer develops—when deciding whether or how to list agents in the report.

NTP scientists may now consider mechanistic data when listing chemicals in the *BRC*, but the criteria do not specifically call for their use, said Norman Drinkwater of the University of Wisconsin at Madison, a member of the NTP Board of Scientific Counselors' ad hoc working group for the review.

In the report, chemicals fall into one of two categories. One category includes known carcinogens, meaning that human studies have produced sufficient evidence to indicate that they cause cancer. The second category includes chemicals that human or animal studies suggest are "reasonably anticipated to be carcinogens." Chemicals in the second category may have increased the incidence of malignant tumors in multiple species or strains of animals or at different dosages or routes of administration. The second category also includes chemicals that induced tumors to an unusual degree with regard to site, type, or age at onset. Chemicals are also placed in the second category if human studies find that they appear to cause cancer but confounding factors are present, such as occupation or smoking.

The NTP Board of Scientific Counselors established an ad hoc working group to review the criteria for listing substances in future *BRC*s. The group met April 24 and 25 in Washington, DC, to hear public comment about the criteria and to prepare recommendations for the full NTP board at a public meeting held June 29–30 at NIEHS.

Members of the ad hoc group favor slightly revising the criteria and including some mechanistic data, according to